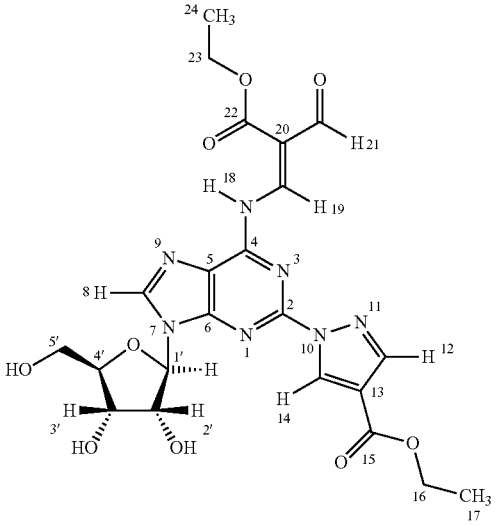
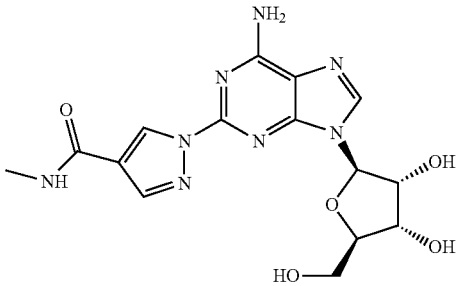
-continued



Minor

EXAMPLE 6

Preparation of (1-{9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-aminopurin-2-yl}pyrazol-4-yl)-N-methylcarboxamide from Compound (4)



Aqueous 40% methylamine solution (1300 ml) was placed in a pressure reactor, cooled to 0-5° C., and the product of Example 5 (ethyl (2E)-3-({9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-2-[4-(ethoxycarbonyl)pyrazolyl]purin-6-yl}amino)-2-formylprop-2-enoate (100 g) added. The mixture was stirred at 0-5° C. for at least 8 hours, monitoring the reaction for completion. When complete, the mixture was warmed, maintaining the temperature between 50 and 60° C. for 1 hour, and then cooled to less than 30° C. over a period of 1 hour. When the temperature was below 30° C., the mixture was degassed using a pressure of 100-150 mm Hg, allowing the temperature to decrease to 0-5° C. The mixture was stirred at 0-5° C. for at least 1 hour, maintaining the pressure at 100-150 mm Hg. The vacuum was then discontinued and replaced by nitrogen, maintaining the temperature at 0-5° C. for not less than 30 minutes. The solid product was then filtered off, washed with water (3×500 ml), then with absolute ethanol (625 ml). The product was dried under vacuum, not allowing the temperature to exceed 40° C., to provide (1-{9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-aminopurin-2-yl}pyrazol-4-yl)-N-methylcarboxamide as its monohydrate.

^{1}H and ^{13}C NMR spectra were obtained in the following manner. Two samples of the material obtained above were weighed out and dissolved in d_6DMSO—5.3 mg was used for the ^{1}H spectra, and 20.8 mg was used for ^{13}C spectra. All spectra were acquired at ambient temperature on a JEOL Eclipse$^+$ 400 spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C.

Label	^{13}C shift (ppm)	^{1}H shift (ppm)	Multiplicity, splitting (Hz)
2	150.5 or 150.3	—	
4	156.4	—	
4a	117.9	—	
6	140.0	8.41	s
7a	150.5 or 150.3	—	
1'	86.9	5.94	D, 6.2
2'	73.7	4.62	m
2'-OH	—	5.50	D, 6.2
3'	70.5	4.17	m
3'-OH	—	5.23	D, 4.7
4'	85.7	3.96	m
5'	61.5	3.67, 3.57	m
5'-OH	—	5.02	D, 5.7
A	140.9	8.07	D, 0.8
B	120.2	—	
C	129.6	8.95	D, 0.8
D	161.7	—	
E	25.6	2.76	D, 4.6
NH_2	—	7.77	br s
NH	—	8.35	Q, 4.6

An elemental analysis gave the following results: C, 43.96%; H, 4.94%; N, 27.94. Theoretical: C, 44.12%; H, 4.94%; N, 27.44%; O, 27.09. The analysis corresponds within experimental error limits to the monohydrate.

We claim:

[1. A pharmaceutical composition prepared from a crystalline monohydrate form of the compound (1-{9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-aminopurin-2-yl}pyrazol-4-yl)-N-methylcarboxamide by adding at least one pharmaceutically acceptable carrier.**]**

[2. The pharmaceutical composition of claim **1**, wherein the monohydrate is substantially free of 2-hydrazinoadenosine.**]**

[3. The pharmaceutical composition of claim **2**, wherein the monohydrate is substantially free of other hydrates or amorphous form.**]**

[4. The pharmaceutical composition of claim **3**, wherein the monohydrate has a purity of at least about 99.6%.**]**

[5. The pharmaceutical composition of claim **4**, wherein the monohydrate exhibits an X-ray powder diffraction pattern having peaks at diffraction angle 2θ (°) of about 6, about 9, about 11, about 13, about 14.5, about 16.5, and about 18 as measured by Cu-Kα1 X-ray powder diffractometry.**]**

6. A pharmaceutical composition of an A_{2A}-adenosine receptor agonist produced by a process comprising the following step:

dissolving a crystalline monohydrate form of the compound (1-{9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-aminopurin-2-yl}pyrazol-4-yl)-N-methylcarboxamide that is substantially free of 2-hydrazinoadenosine in a pharmaceutically acceptable carrier.

7. The pharmaceutical composition of claim 6, wherein the crystalline monohydrate is substantially free of other hydrates or amorphous forms.

8. The pharmaceutical composition of claim 6, wherein the crystalline monohydrate has a purity of at least about 99.6%.